

Perspectives

# Lung cancer screening: the hidden public health emergency

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#### Key points

- Lung cancer is the most common cause of cancer death in Australia and worldwide. Lung cancer screening (LCS) with low-dose computed tomography (LDCT) reduces lung cancer mortality in high-risk groups by detecting early, curable disease
- A targeted LCS program, combined with smoking-cessation treatment, could be cost-effective in Australia
- Careful planning for recruitment and participant care will be needed to ensure equity of access to LCS across all highrisk groups
- LCS could also act as a "health check" to detect other diseases via LDCT
- Disadvantaged groups at high risk of lung cancer require equity of access to LCS

#### Abstract

Lung cancer causes nearly 2 million deaths per year worldwide, and cases continue to rise. Most lung cancer is diagnosed at late, incurable stages, and the five-year survival is a fraction of that for other common cancers, including breast, prostate, melanoma and colorectal cancer. Lung cancer screening (LCS) in high-risk populations using low-dose computed tomography (LDCT) could potentially save thousands of lives per year by shifting the stage at diagnosis to early curable disease. Although an LCS program has not yet started in Australia, two trials have provided local data on the feasibility, selection criteria and outcomes. A government-commissioned report has detailed a potential national program, and Federal Budget funding has been committed to early feasibility projects that include population-specific consultations with, for example, Aboriginal and Torres Strait Islander communities who are at higher risk of lung cancer due to high smoking rates. Effective recruitment to LCS, embedded smoking cessation and the provision of subsequent lung cancer care to all at-risk Australians remain key priorities for any future LCS program.

#### The hidden impact of lung cancer

Lung cancer causes the most cancer deaths worldwide in both men and women with nearly 2 million deaths per year. More than 13 000 new cases are diagnosed annually in Australia, with lung cancer causing nearly 20% of all cancer deaths annually.<sup>1</sup> Most lung cancer cases in Australia are advanced, with fewer than 20% of cases diagnosed early. The five-year survival rate is approximately 20%. Delayed presentation may relate to factors such as under-appreciation of symptoms and feelings of stigma and guilt. In contrast, other common cancers (detected at early stages) have much better outcomes, with current five-year survival rates of 92% for breast cancer, 96% for prostate cancer, 92% for melanoma and 70% for colorectal cancer (CRC).<sup>2</sup>

# The case for lung cancer screening

Recent advances in therapy have led to modest improvements in lung cancer survival. A significant jump in early detection is urgently needed. Smoking cessation and education on lung cancer symptoms are vital but will only improve survival after decades. LCS may be our most powerful tool to reduce lung cancer mortality rapidly. Two landmark randomised trials of LDCT have demonstrated significant stage shift and resulted in 20– 24% reductions in mortality due to lung cancer with LCS in targeted, high-risk populations<sup>3,4</sup> (defined as people aged 50–75 and who currently smoke or have quit in the past 15 years). Integration of other health prevention strategies, especially smoking cessation, amplifies the impact of screening with vastly improved survival in screening participants who also stop smoking.<sup>5</sup>

A distinct shift to earlier stage diagnosis has accompanied LCS in the US. Early diagnosis means curative treatment is possible; the effective introduction of LCS could profoundly improve outcomes for thousands of Australians. Screening has led to survival improvements in other major cancers, such as breast<sup>6</sup> and colorectal cancer, both of which have screening programs in Australia. If implemented in Australia, an LCS program is projected to save 12 000 lives in the first ten years.<sup>7</sup>

# A vision for lung cancer screening in Australia

Australia does not have LCS, but momentum is building for change.<sup>8</sup> Australian researchers have trialled LCS in high-risk participants with a history of tobacco smoking in two studies: the Queensland Lung Cancer Screening Study<sup>9</sup> and the International Lung Screen Trial.<sup>10</sup> The Australian Federal Government commissioned Cancer Australia to report on a potential national LCS program, with the report published in late 20207 concluding that LCS "would enable unprecedented changes in clinical management and address the poor outcomes...for lung cancer that have been observed over many years".7 Lung Foundation Australia<sup>11</sup> has strongly advocated for lung cancer care with particular focus on equity of access. The draft National Tobacco Strategy 2022-203012 prioritises prevention of smoking uptake and evidencebased cessation strategies, which (if embedded in LCS) improve mortality benefit and cost-effectiveness of LCS. In May 2021, the Federal Government committed A\$6.9 million to early scoping work for LCS, including stakeholder consultation, extensive engagement and codesign with Aboriginal and Torres Strait Islander peoples

who experience disproportionately poor outcomes for lung cancer.

The cost-effectiveness of cancer screening is complex for lung cancer and other cancers. The models used to estimate the costs of LCS are evolving rapidly. Earlier modelling calculated LCS in Australia as relatively expensive, although more recent costings were much lower.<sup>7</sup> While novel therapies, such as immunecheckpoint inhibition and targeted agents, have led to improvements in disease response and outcomes, risk factor reduction and screening for early-stage disease may have more powerful effects on survival and avoid the high costs of systemic medication for advanced disease. Smoking cessation interventions in LCS improve costeffectiveness.<sup>13</sup>

All cancer screening programs must fulfil criteria set out in the principles of the Australian Government's Population-Based Screening Framework<sup>14</sup> for key health problems, effective tests, the safety of follow-up, effective early treatment and minimal adverse effects of the screening process. Lung cancer is an important health problem; the screening test (LDCT) has been shown to be clinically effective in targeted high-risk groups and has a real-world impact, now evident in the US. Targeted LCS is acceptable in international trial settings and realworld programs in the US<sup>15</sup>, Canada<sup>16</sup>, South Korea<sup>17</sup> and Taiwan.<sup>18</sup> Treatments for early-stage lung cancer are widely available and produce much better survival than treatment for advanced disease. The potential harms of LCS, including overdiagnosis, false-positive findings and unnecessary investigations, can be minimised with careful selection of participants<sup>9</sup> and evaluation of lung nodules.10

Positive "knock-on" effects across the health system may come from the introduction of LCS with the acceleration of preventative health policies, including those outlined in the National Preventive Health Strategy 2021–2030.<sup>19</sup> In addition, if readily available to high-risk groups, LCS could help overcome the inequity of access that these groups face for lung cancer treatment. This could benefit rural and remote patients, those without access to multidisciplinary teams<sup>20</sup> and could reduce the potential for stigma to delay the seeking of treatment.

Strategies encouraging participants to enrol in LCS (e.g. pre-booked appointments, information brochures and videos) have had excellent uptake with up to 52% participation rates reported in a British study<sup>21</sup> compared with, for example, much lower rates reported in the US, ranging from 2-9%.<sup>22</sup> Poor uptake has prompted the US Preventive Services Taskforce to broaden eligibility criteria to minimise sex, race and ethnic-based disparities in screening uptake. Since the screening was recommended, a shift to diagnosing early-stage disease in US populations is already evident (from 20% in 2013 to 28% in 2018).<sup>23</sup> Participation in UK pilot LCS studies have proven highly effective in reaching people who smoke and live in lower socioeconomic communities.<sup>24</sup>

LCS participant selection is more accurate using multivariable risk assessment tools, such as the  $PLCO_{m2012}$  model used in the International Lung Screening Trial (ILST)<sup>10</sup> rather than the categorical eligibility criteria of age and smoking status used in the key trials. Personalised risk calculators present an opportunity to empower individuals to identify whether they are at risk for lung cancer, can be offered online and can prompt individuals to consult their general practitioner. Effective integration of primary health care into screening programs will require support and educational materials for healthcare providers and potential participants.

## Integration of lung cancer screening into comprehensive public health prevention

A national LCS program has the potential to combine several approaches to health prevention. We outline two immediate opportunities for public health to capitalise on the test and the condition. Firstly, LCS results could be harnessed as a means for lung health screening and detect the early onset of other diseases. Unlike other cancer screening programs, where the test measures a specific finding, LDCT chest scans canvass a large area of the body. As well as lung nodules, other findings could include pulmonary abnormalities<sup>25</sup> (emphysema, fibrosis, inflammation), osteoporosis<sup>26</sup>, coronary artery disease and cardiac valve disease.<sup>25</sup> This provides an opportunity to use LDCT screening to evaluate asymptomatic individuals for other health conditions. However, adversely, this could also lead to overdiagnosis, additional harmful tests, unnecessary costs and patient concern, depending on the incidental findings.

Smoking cessation offered at multiple points in the screening pathway can markedly improve lung cancer outcomes. Tobacco treatment clinics could provide referral pathways for LCS, enhancing access for disadvantaged groups. Secondly, established cancer screening programs could combine strategies using risk-stratification tools to target high-risk populations. With integration and restructuring, cancer screening programs for breast, bowel, cervical and lung cancers and melanoma could streamline referral pathways and maximise health prevention for participants. South Korea's National Cancer Screening Program currently provides screening for five common cancers (stomach, liver, colorectal, breast and cervical<sup>27</sup>) and will soon incorporate LCS following a successful trial.<sup>17</sup>

# **Future directions**

A potential LCS program in Australia proposes targeting high-risk groups, initially, people aged 50–70 who currently smoke or have a history of smoking of at least 30 pack-years or have quit in the past 10 years.<sup>8</sup> However, eligibility may change in the future to include other factors such as genetic risk or environmental exposures. An LCS program must be agile, adjusting to changes in screening tests and technologies (akin to the National Cervical Screening Program) to incorporate biomarkers, artificial intelligence and other emerging risk factors.<sup>28</sup>

A resilient LCS program calls for durable healthcare infrastructure. Material requirements will include computed tomography (CT) scanners, follow-up clinics, robust communications and a well-trained workforce to meet demand. Software requirements will consist of clearly defined minimum datasets, integrated clinical guality registries and well-defined follow-up pathways. Successful promotion, high participation rates and healthcare practitioner engagement will also determine the impact of LCS programs. Participants with a positive finding will require meticulous clinical care across public and private healthcare services. This includes accurate lung nodule evaluation, management of incidental and efficient referral pathways for participants with positive scans. Pathways will need to adapt for people whose risk status changes over time, including developing criteria for "exiting" LCS, such as age, comorbidity, fitness for treatment and personal preference.

Reducing the world's leading cause of cancer mortality needs commitment from policy decision-makers. An Australian LCS program may lead to rapid additional and translatable health benefits based on the broad reach of the screening test and the impact of shared risk factors. If Australia introduces a targeted LCS program, we will have remarkable opportunities to improve and integrate public health infrastructure and effectively involve primary care to improve the health of the most disadvantaged Australians.

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ES is a member of the Thoracic Oncology Group of Australasia Board. She is a member of the Australian Lung Cancer Conference Steering Committee 2023; is Convenor, TSANZ Tobacco Control Special Interest Group (2021–present) and Co-Chair of the Lung Cancer Research Network, Woolcock Institute of Medical Research (2019–present). She has also held roles of Group Head, Asia Pacific Society of Respirology (2020–2021); Head, Asia Pacific Society of Respirology Lung Cancer Assembly (2019–2021). These are all nonremunerated positions.

HM is a member of the Lung Foundation Australia (LFA) Lung Cancer BluePrint 2.0 Expert Working Group; a stakeholder member of Cancer Australia's Lung Cancer Screening Workshops; and a member of the LFA Australian Lung Cancer Conference (ALCC 2023) Organising Committee. These are all non-remunerated positions.

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### **Competing interests**

ES has provided expert testimony for Pinnacle Healthcare and reports payment for lectures from Astra Zeneca, MSD and The Limbic.

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### Author contributions

All authors contributed to the manuscript's concept, writing and final approval.

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